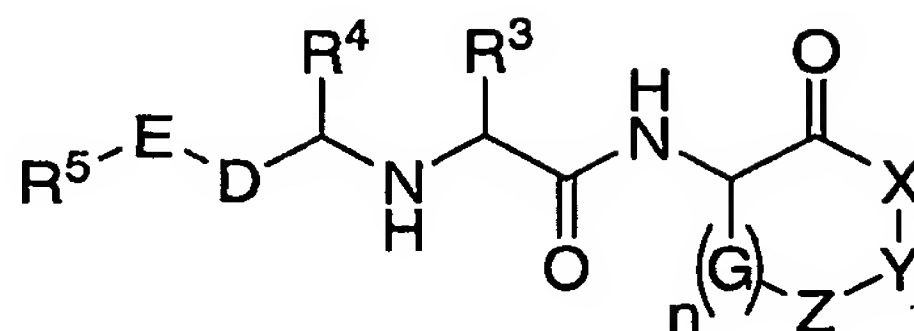


WHAT IS CLAIMED IS:

1. A compound of the formula:



- 5 wherein X is O or -NR⁹;
 Y is CR¹R², -SO₂, C=O or -NR⁹;
 Z is CR¹R², O, S, -SO₂ or -NR⁹;
 Each G is independently CR¹R²;
- 10 R¹ is hydrogen, halo, or C₁₋₆ alkyl which is optionally substituted with one, two, or three substituents independently selected from halo or -OR⁸;
- R² is hydrogen, halo or C₁₋₆ alkyl which is optionally substituted with one, two, or three substituents independently selected from halo or -OR⁸;
- 15 or R¹ and R² can be taken together with the carbon atom to which they are attached to form a C₃₋₈ membered ring which is optionally substituted with one or two substituents independently selected from C₁₋₆ alkyl, halo or keto;
- 20 R³ is C₁₋₆ alkyl or C₂₋₆ alkenyl, wherein said alkyl and alkenyl groups are optionally substituted with C₃₋₆ cycloalkyl, aryl, heteroaryl or one to six halo;
- R⁴ is C₁₋₆ alkyl substituted with 1-6 halo;
- 25 D is aryl or heteroaryl, wherein said aryl or heteroaryl group, which may be monocyclic or bicyclic, is optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁₋₆ alkyl, haloalkyl, halo, keto, alkoxy, -SR⁶, -OR⁶, N(R⁶)₂ or -SO₂R⁶
- E is aryl or heteroaryl, wherein said aryl or heteroaryl group, which may be monocyclic or bicyclic, is optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C₁₋₆ alkyl, haloalkyl, halo, keto, alkoxy, -SR⁶, -OR⁶, N(R⁶)₂ or -SO₂R⁶;
- 30

R^5 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy, aryl, heteroaryl, C_{3-8} cycloalkyl, heterocyclyl, $-OR^6$, $-C(O)R^6$, $-R^7C(O)R^6$, $-C(O)N(R^a)(R^b)$, $-C(O)N(R^9)(R^9)$, $-C(R^7)(R^8)OH$, R^7SR^6 , $-C(R^a)(R^b)N(R^6)_2$, $C(R^a)(R^b)N(R^a)(R^b)$, $-NR^7C(O)NR^7S(O)_2R^6$, $-SO_mR^6$, $-SO_2N(R^a)(R^b)$, $-SO_2N(R^7)C(O)(R^9)$, $-SO_2(R^7)C(O)N(R^9)_2$, $-N(R^7)C(O)N(R^7)(R^6)$, $-N(R^7)C(O)R^6$, $-N(R^7)C(O)OR^7$, $-N(R^7)SO_2(R^7)$, $-C(R^a)(R^b)SC(R^a)(R^b)(R^6)$, $-C(R^a)(R^b)NR^7C(R^a)(R^b)(R^6)$, $-C(R^a)(R^b)NH_2$, $-C(R^a)(R^b)C(R^a)(R^b)N(R^a)(R^b)$, $-C(O)C(R^a)(R^b)N(R^a)(R^b)$, $-C(R^a)(R^b)N(R^6)C(O)R^6$, $-C(R^a)(R^b)C(O)N(R^a)(R^b)$, wherein said groups are optionally substituted on either the carbon or the heteroatom with one to five substituents independently selected from C_{1-6} alkyl, halo, keto, cyano, haloalkyl, hydroxyalkyl, $-OR^6$, $-NO_2$, $-NH_2$, $-NHS(O)_2R^8$, $-R^6SO_2R^9$, $-SO_mR^7$, heterocyclyl, aryl, or heteroaryl;

R^6 is selected from hydrogen, C_{1-6} alkyl, aryl, aryl(C_{1-4})alkyl, heteroaryl, heteroaryl(C_{1-4})alkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkyl(C_{1-4})alkyl, and heterocyclyl(C_{1-4})alkyl wherein said groups can be optionally substituted with one, two, or three substituents independently selected from halo, alkoxy, cyano, $-NR^aR^b$, $-SR^a$ or $-SO_mR^a$;

R^7 is hydrogen or C_{1-6} alkyl;

R^8 is hydrogen or C_{1-6} alkyl;

R^9 is hydrogen, C_{1-6} alkyl, $C(O)R^7$, $C(O)C_{1-6}$ alkyl, $C(O)aryl$, $C(O)heteroaryl$, $C(O)C_{1-6}$ alkoxy, $SO_2(C_{1-6}$ alkyl), $SO_2(aryl)$ or $SO_2(heteroaryl)$, wherein said alkyl groups are optionally substituted with one, two, or three substituents independently selected from halo, alkoxy, cyano, $-NR^7$ or $-SR^7$;

R^a is hydrogen or C_{1-6} alkyl which is optionally substituted with one, two, or three substituents independently selected from halo or $-OR^6$;

R^b is hydrogen or C_{1-6} alkyl which is optionally substituted with one, two, or three substituents independently selected from halo or $-OR^6$;

or R^a and R^b can be taken together with the nitrogen atom to which they are attached or are between them to form a C_{3-8} heterocyclyl ring which is optionally substituted with one or two substituents independently selected from C_{1-6} alkyl, halo hydroxyalkyl, hydroxy, alkoxy or keto;

n is an integer from zero to two;

m is an integer from zero to two;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. The compound of Claim 1 wherein R³ is C₁₋₆ alkyl optionally substituted with
5 one to six halo.

3. The compound of Claim 2 wherein D is aryl.

4. The compound of Claim 3 wherein D is phenyl.

5. The compound of Claim 2 wherein E is aryl or heteroaryl, wherein said aryl or
heteroaryl group is optionally substituted on either the carbon or the heteroatom with one to five halo.

6. The compound of Claim 5 wherein E is phenyl or pyridyl, wherein said phenyl
15 or pyridyl group may be substituted with one to five halo.

7. The compound of Claim 1 selected from
N¹-(2-oxotetrahydrofuran-3-yl)-N²-{(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethyl}-L-
leucinamide;
20 N¹-[2-oxo-1-(phenylsulfonyl)pyrrolidin-3-yl]-N²-{(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-
yl]ethyl}-L-leucinamide;
N²-((1S)-1-{4'-[1-(aminocarbonyl)cyclopropyl]biphenyl-4-yl}-2,2-difluoroethyl)-4-fluoro-N¹-[(3S,4S)-2-
oxo-4-(trifluoromethyl)pyrrolidin-3-yl]-L-leucinamide;
N²-{(1S)-2,2-difluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]propyl}-4-fluoro-N¹-[(3S)-2-oxo-4-
25 (trifluoromethyl)tetrahydrofuran-3-yl]-L-leucinamide;
N²-((1S)-1-{4'-[1-(aminocarbonyl)cyclopropyl]biphenyl-4-yl}-2,2-difluoroethyl)-4-fluoro-N¹-[(3S,4S)-4-
methyl-2-oxo-1-(pyridin-2-ylmethyl)pyrrolidin-3-yl]-L-leucinamide;
N²-((1S)-1-{4'-[1-(aminocarbonyl)cyclopropyl]biphenyl-4-yl}-2,2-difluoroethyl)-N¹-[(3R)-4,4-difluoro-2-
oxopyrrolidin-3-yl]-4-fluoro-L-leucinamide;
30 N¹-(2-oxopyrrolidin-3-yl)-N²-{(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethyl}-L-
leucinamide;
N¹-[(3S)-1-(methylsulfonyl)-2-oxopyrrolidin-3-yl]-N²-{(1S)-2,2,2-trifluoro-1-[4'-
(methylsulfonyl)biphenyl-4-yl]ethyl}-L-leucinamide;
N¹-[2-oxo-1-(phenylsulfonyl)pyrrolidin-3-yl]-N²-{(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-
35 yl]ethyl}-L-leucinamide;

*N*¹-[2-oxo-5,5-bis(trifluoromethyl)tetrahydrofuran-3-yl]-*N*²-{(1*S*)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethyl}-*L*-leucinamide;

*N*¹-(5,5-dimethyl-2-oxotetrahydrofuran-3-yl)-*N*²-{(1*S*)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethyl}-*L*-leucinamide;

5 or a pharmaceutically acceptable salt or stereoisomer thereof.

8. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.

10 9. A process for making a pharmaceutical composition comprising combining a compound according to Claim 1 and a pharmaceutically acceptable carrier.

15 10. The use of a compound of Claim 1 for the preparation of a medicament useful in the treatment of: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, atherosclerosis, obesity, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma, in a mammal in need thereof.

20 11. A pharmaceutical composition comprising a compound of Claim 1 and another agent selected from: an organic bisphosphonate, an estrogen receptor modulator, an estrogen receptor beta modulator, an androgen receptor modulator, an inhibitor of osteoclast proton ATPase, an inhibitor of HMG-CoA reductase, an integrin receptor antagonist, or an anabolic agent, a selective cyclooxygenase-2 inhibitor, or a pharmaceutically acceptable salt or mixture thereof.

25 12. The use of a composition of Claim 11 in the preparation of a medicament useful in the treatment of: osteoporosis, glucocorticoid induced osteoporosis, Paget's disease, abnormally increased bone turnover, periodontal disease, tooth loss, bone fractures, atherosclerosis, obesity, rheumatoid arthritis, osteoarthritis, periprosthetic osteolysis, osteogenesis imperfecta, metastatic bone disease, hypercalcemia of malignancy or multiple myeloma, in a mammal in need thereof.

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